PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference K 3151	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/09247	International filing date *(day/month/year)* 20.08.2003	Priority date *(day/month/year)* 23.08.2002
International Patent Classification (IPC) or both national classification and IPC A61P35/00		
Applicant DEUTSCHES KREBSFORSCHUNGSZENTRUM STIFTUNG DES....		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.03.2004	23.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer van der Kooij, M Telephone No. +31 70 340-4606

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09247

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-14 as originally filed

Claims, Numbers

1-12 as originally filed

Drawings, Sheets

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 9-11

   because:

   ☒ the said international application, or the said claims Nos. 9-11 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-12
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-12
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-8 and 12
	No:	Claims	(see seperate sheet)

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III-1). Rule 67.1(iv) PCT and Article 34(4)(a)(I) PCT).

Claims 9-11 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V-1). Rule 66.1(e) PCT.

The Applicant's attention is drawn to the fact that the present opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up, i.e. pharmaceutical compositions comprising formula (I) optionally combined with cyclosporine, rapamycin, 15-deoxyspergualine, OKT3, azathioprine, cytokines, interferon and further cytostatic agents and their use for treating a cancerous disease or an autoimmune disease.

V-2). Prior art documents:

V-2.1). The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: WO-A-0010543
D2: US5679697
D3: JP-A-11060493 (cited as Derwent abstract, AN: 1999-226104)

V-2.2). D1 is considered to represent the most relevant state of the art and discloses medicaments comprising complexed platinum compounds and combination preparations thereof for treating cancer (see claims 1-11).

V-3). Article 33(2) PCT.

No prior art document discloses a pharmaceutical preparation comprising at least one compound of general formula (I) or its process for its preparation or its use in relation to the treatment of cancerous disease, in particular parvocellular bronchial carcinoma or colorectal carcinoma, or in relation to the treatment of autoimmune disease.
As a consequence, the subject-matter of claims 1-12 fulfills the requirements of Article 33(2) PCT.

V-4). Article 33(3) PCT.

V-4.1). The pharmaceutical compositions according to claims 1-8 and its preparation according to claim 12 are considered to be inventive.
V-4.2). The use of compounds according to formula (I) in relation to the use in cancer therapy is considered to involve an inventive step, because of the following reasons:
D1 is considered to represent the most relevant state of the art and discloses medicaments comprising complexed platinum compounds and combination preparations thereof for treating cancer (claims 1-11). The subject-matter of claims 1-10 and 12 differs in that the platinum is exchanged for the palladium.
The problem to be solved in claims 9 and 10 can therefore be regarded as the provision of a more effective medicament for treating cancer.
The solution proposed by the applicant is the use of compounds according to formula (I), allowing an increased effectiveness and low toxicity which enables the maximum tolerable dose to be applied.
D1 does not contain any incentive to use non-platinum metal agent.
D2 does not indicate that any other palladium complexes, in particular xanthogenate complexes might be effective against tumours.
D3 teaches the use of a combination of palladium and platinum colloids and is silent about the effect of palladium alone or complexed with xanthogenates.
Thus, the prior art documents give no incentive to use palladium xanthogenate complexes in cancer therapy. Moreover, the skilled person would not have expected to obtain compounds with a significant higher anti-tumour effectiveness by exchanging platinum with palladium in a platinum xanthogenate complex. Thus, claims 9 and 10 are considered to involve an inventive step.
As a matter of facts, no medical use of palladium xanthogenate complexes was known.
Hence, the subject-matter of claims 1-12 involve an inventive step and satisfy the criterion set forth in Article 33(3) PCT.

V-5). Article 33(4) PCT.

V-1). Claims relating to pharmaceutical preparations according to claims 1-8 are product claims and are generally considered as industrial applicable since they can be made or used in industry or agriculture. For similar reasons, a process for preparation for the production of said pharmaceutical preparations (claim 12) is considered as industrial applicable. Therefore, claims 1-8 and 12 are considered to fulfill the requirements of Article 33(4) PCT.

V-2). For the assessment of the present claims 9-11 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Further remarks relating to Article 6 PCT.

The expression "these residues being optionally substituted by one or several substituents" in claim 1 is considered to be unclear contrary Article 6 PCT since the substituted substituents are not defined.

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